1. *Does the RFA for establishing Centers of Cancer Nanotechnology Excellence (CCNEs; RFA-CA-05-024) support Investigative New Drug (IND) applications and clinical trials?*

   No. This RFA funds research from discovery through preclinical trials. The NCI wishes to focus on the development of new technologies and approaches. NCI resources and programs that support clinical trials include the Early Detection Research Network (EDRN; http://edrn.nci.nih.gov) and the Development of Clinical Imaging Drug Enhancers (DCIDE) initiative available through the Cancer Imaging Program (http://imaging.cancer.gov/).

2. *Can proposals submitted in applications for RFA-CA-05-024 link to existing U54 clinical trials?*

   Yes.

3. *How much of an applicant's proposed CCNE budget should be directed to Core Resources versus the support of individual projects?*

   The budget strategy for CCNE proposals differs from that of Cancer Center proposals in that the bulk of resources should be directed to individual research projects. Where possible, applicants are encouraged to leverage existing resources and support from Cancer Centers and other programs.

4. *Why is the RFA for Cancer Nanotechnology Platform Partnerships (RFA-CA-05-026) an R01 research project grant instead of an R21 or R21/R33 phased innovation award?*

   The NCI offers phased innovation approaches for many technology-based RFAs, including those featured in the Innovative Molecular Analysis Technologies (IMAT; http://otir.cancer.gov/tech/imat.html) and Cancer Imaging Programs (http://imaging.cancer.gov/). The R01 mechanism allows the NCI the flexibility to review smaller initiatives below the level of the fully-developed Center. The NCI has used the R01 mechanism to fund technology development through Bioengineering Research Partnerships and Bioengineering Research Grants (BRPs and BRGs; http://searchl.nci.nih.gov/tech/bioengineering_initiatives.html).

5. *Can you clarify what is meant by the requirement for "nanomaterials fabrication/synthesis facilities and/or capabilities" in RFA-CA-05-024?*

   Synthesis capability is an essential requirement for applications. For a CCNE, the NCI seeks evidence of capabilities for engineering and manufacturing at the nanoscale level. The language of the RFA is intentionally broad to retain flexibility and encourage a diversity of approaches. Specific questions regarding an applicant's nanomaterials fabrication capabilities should be directed to the NCI while the application is being developed.

6. *Must the applicants for Centers of Cancer Nanotechnology Excellence (CCNEs; RFA-CA-05-024) partner with an NCI Comprehensive Cancer Center?*

The RFA requires collaboration with any NCI-designated cancer center (see http://www3.cancer.gov/cancercenters/centerslist.html).

7. *Can the fundamental materials in projects proposed in response to these RFAs include nucleic acids or peptides?*

   Yes. Biological agents are one category of acceptable components for proposed materials. However, from a synthesis perspective, the NCI encourages the use of inorganic materials.

8. *If an applicant has equipment that features the option of purchasing FDA-approved software (e.g., FDA-upgrade level light-scattering software for sizing of nanoparticles), should this be included in the budget?*

   The NCI recognizes the breadth of technical supplies and equipment needed to conduct nanotechnology research for cancer, and the Institute does not wish to prescribe specific rules for the inclusion or exclusion of specific equipment purchases. Rather, the Institute recommends that applicants justify all budgetary items and tie them into preclinical milestones in their applications.

9. *For the purpose of these RFAs, is it acceptable to use multiple nanotechnology platforms in focused efforts toward one cancer type?*

   While the NCI seeks breadth of technologies and their application to cancer processes, rather than to specific cancer sites, the Institute does not discount this approach. Reviewers will likely consider the impact of the composite of technologies proposed as they address the six areas of focus specified in the RFAs. Applicants wishing to use such strategies are encouraged to justify their cases.

10. *Can an applicant use these RFAs to request funds to support a drug formulation?*

    Yes. This should be included in the budget for synthesis/fabrication components.

11. *In Section IV.2, "Content and Form of Application Submission," the PHS 398 application form stipulates a maximum of 25 pages for the description of projects. Is this the total allotment for all projects included in the RFA or the total per individual project?*

    The application allows 25 pages of description per individual project. An application for a CCNE will feature 5-8 projects, each of which may have up to 25 pages of description.

12. *Should applications for CCNEs feature a level of focus and integration suggestive of a P01 application, or can the Center consist of investigators who share technology and reagents but do not present the level of integrated focus required for a P01 application?*

    The NCI does not have a preset threshold for investigator integration for the CCNEs. An applicant should make a case to reviewers that he or she has the correct degree of integration for the projects proposed.

13. *When evaluating a nanotechnology in animal models, to what degree will reviewers weight the choice of model?*

    Reviewers will look for the use of models or relevant cancer cell lines and resources that are appropriate to the projects proposed. NCI expects that applicants will use the most representative, well-documented models to serve in conducting the proposed studies addressing key cancer biology questions. For example, refer to the Mouse Models of Human Cancer Consortium (MMHCC) (http://emice.nci.nih.gov/).

14. *What are key requirements and suggestions regarding data sharing and intellectual property (IP) issues?*

    As part of the data sharing plan, applicants should include a timeline for the sharing of data. From a patent perspective, IP should be in place prior to sharing, and the Institute recommends the filing of patent applications prior to public disclosure of data.

15. *Should applicants utilize available Core facilities at the Comprehensive Cancer Centers that are engaged in pharmacokinetic/pharmacodynamic studies, or should they instead submit developed nanotechnologies to the Nanotechnology Characterization Laboratory (NCL) for standardization?*

    The NCI encourages applicants to leverage local capabilities whenever possible to advance individual projects. Members of the NCL steering committee are currently developing a set of criteria for submission to the NCL.

16. *In Part A, the designated page limit is 40 pages. What about PI bios, etc.? Does the 40-page limit refer to the program description or budget justification stuff?*

    The limit is inclusive of all materials. Only PI bios should be included; other collaborative staff bios may be placed in an appendix.

17. *Will reviewers be looking for R01-style projects or R21-style projects for these RFAs?*

    In general, the NCI wants to see a phased innovation concept in terms of how projects are outlined. The Institute will provide reviewers with examples of desired project types and structures to guide the review process. Applicants must include specific, quantitative milestones for each proposed project.

18. *Regarding milestones, is it acceptable to present up to 3 years of milestones?*

    This is acceptable for individual projects, in which specific aims and metrics are required. Overall programmatic milestones and how these milestones meet with thematic areas are required for the CCNEs. In applications, the NCI is looking to see how decisions are going to be made about individual projects within Centers.

19. *Does the individual Center Steering Committee within a CCNE decide on the fate of individual projects?*

    Yes, along with the NCI and the overall CCNE Coordinating and Governance Committee. Proposed projects will be assessed by the committees on an on-going basis, and adjustments in effort and focus will be made in accordance with the progress of a given project.

20. *Can you provide details of the review process for CCNE applications (e.g., the number of reviewers per application)?*

    Due to the scope and complexity of applications, it is unlikely that one reviewer will manage all projects within a given application. Rather, each reviewer will read portions of several applications and assign initial tentative scores for the specific sections. However, each application will be assigned a "lead" reviewer, who will lead discussions among the team of reviewers who have evaluated various sections and/or projects within the application. This discussion leader shall be familiar with the overall application, although he or she may have reviewed sections of it in great detail. These discussions will result in a final recommended score to the National Cancer Advisory Board.

21. *What level of preliminary results will be necessary to make an application competitive? Are all projects within an application expected to have attained the same level of preliminary results, or can these levels vary?*

    The NCI recognizes that these levels will vary between projects, as some proposed projects may involve higher risk, or be in earlier stages of development, than others. However, the Institute seeks a portfolio of programs that integrate well and address cancer biology processes. The inclusion of several high-risk projects is welcomed; however, a management structure within a Center that indicates the procedures to be followed in the event of an unsuccessful project is essential. The NCI wishes to stimulate highly creative approaches. Therefore, the Institute has no preconceived notion of the number of projects that should have already reached a certain stage of maturity at the time of submission. It is also acceptable and expected to propose several projects that have time limits shorter than five years, so long as these are justified and a plan is provided for events that will follow the completion of shorter projects.

22. *A stated requirement for CCNE applicants is "technology assessment capabilities to identify new nanomaterials for development." Can you clarify what is meant by this requirement?*

    Because nanotechnologies are evolving rapidly, the NCI seeks evidence that a CCNE is continually seeking new and creative approaches. CCNEs should demonstrate the capacity and flexibility to adapt to and include new technologies when appropriate, even those not developed within the organizations comprising that Center when relevant experimental opportunities warrant doing so. While recognizing that such adaptations and inclusions will change the ways that CCNEs will look over time, the Institute seeks demonstrated evidence that a Center has a forum or committee that actively seeks those new approaches that will optimize a platform as the technologies evolve.

23. *Can a stand-alone project that does not directly use a nanoparticle (e.g., the generation of a common knowledge base necessary to use and apply nanotechnology platforms) be included in a CCNE application?*

    Yes. Such a project could fall within the category of "research enablers." However, inclusion of such projects must be justified within the context of other proposed projects.

24. *According to information provided about the NCI Nanotechnology Characterization Laboratory (NCL), why are only those particles smaller than 100 nm deemed suitable for characterization?*

    The NCI Nanotechnology Characterization Laboratory (http://ncl.cancer.gov) will consider larger particles for characterization on an individual basis. The size of the particle should not be considered as a rate-limiting factor for submission to the NCL.

25. *Can shared resources already in place at NCI Specialized Programs of Research Excellence (SPOREs) be included in applications for CCNEs?*

    Where possible, the NCI encourages leveraging of existing resources rather than creating a free-standing program. Therefore, applicants are encouraged to be guided by the science and technology to create a reasonable balance between existing and new resources.

26. *How extensive should the training portion of the CCNE application be?*

    The NCI has a responsibility to educate the public and next generation of scientists with respect to efforts in cancer nanotechnology. While the Institute does not prescribe a format for community education or research scientist training programs, reviewers of CCNE applications will look for innovative ways to expose students to research efforts in this field and to educate the public. While such strategies may be in the developmental stages at present, the Institute encourages creative ideas that may be formalized at a later point in time.

27. *What are the NCI's expectations for industry involvement in the Alliance for Nanotechnology in Cancer?*

    The Institute highly encourages industry partners to participate in individual projects, applications, and on the Teaming Website (http://nano.cancer.gov/funding_teaming_site.asp). At the site, registered private sector entities can offer technologies, facilities, equipment, sponsorship of training meetings, and other items for consideration in partnerships and teams.

28. *Can a facility submitted as a Core facility in a CCNE RFA application be located outside of an NCI-designated Cancer Center?*

    Yes.

29. *Can a for-profit entity serve as a Core in a CCNE RFA application?*

    Yes.

30. *Must the PI on a CCNE application be an investigator at an NCI-designated Cancer Center?*

    No.

31. *Can applicants request to set aside funds that are not allocated to any specific project described in one of these RFAs?*

    While the NCI seeks to build flexibility into these RFAs, undescribed functions may pose difficulties for reviewers. The Institute suggests modular grants for such proposals.